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Researches upon the *Ætiology*
of Idiopathic Epilepsy.

A Preliminary Communication.

BY

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System, New York Polyclinic,

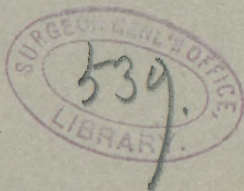
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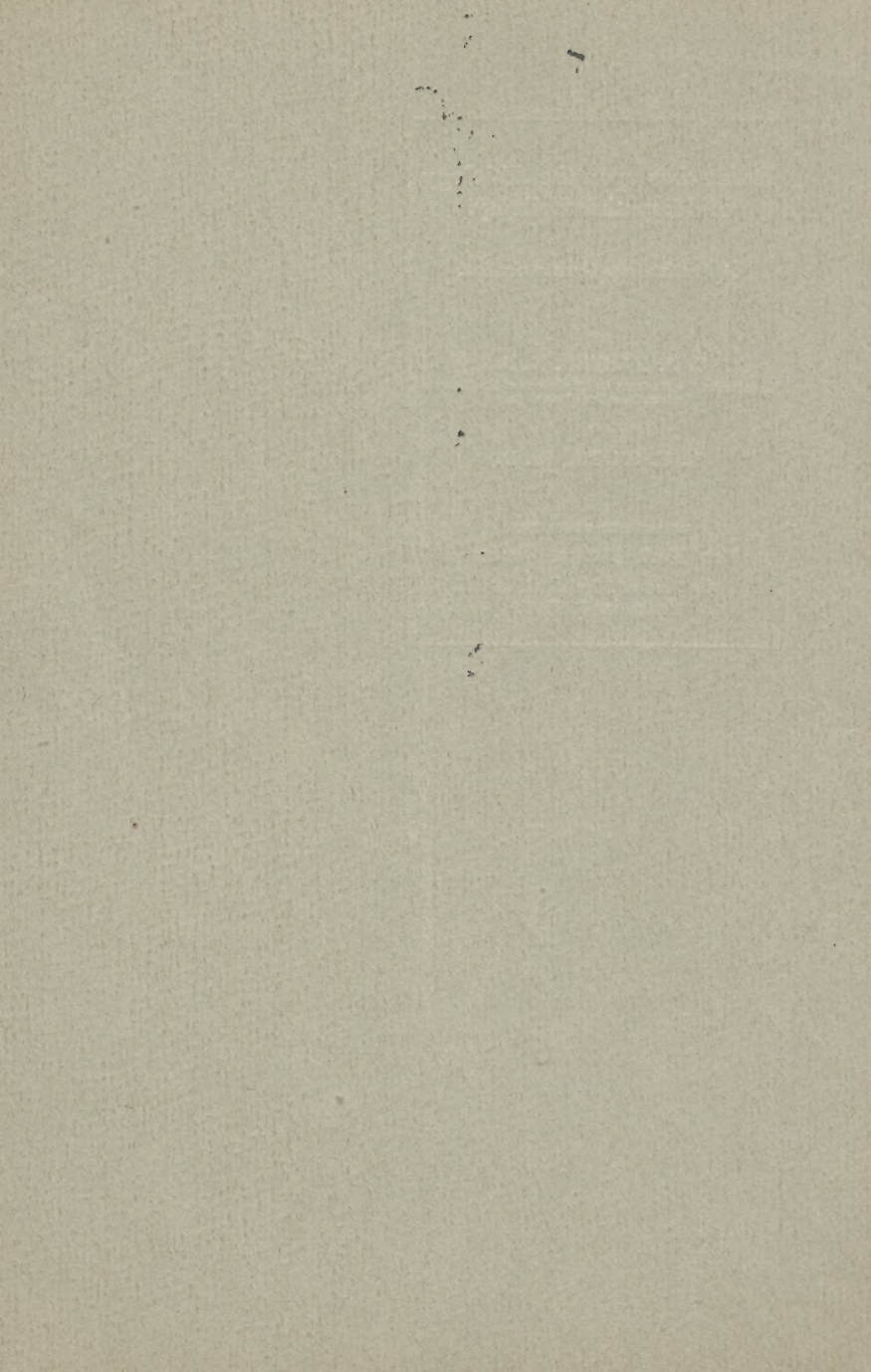
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REPRINTED FROM THE

New York Medical Journal

*for August 20 and 27, and
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RESEARCHES UPON THE
ÆTIOLOGY OF IDIOPATHIC EPILEPSY.

*A PRELIMINARY COMMUNICATION.**

BY C. A. HERTER, M. D.,

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NEW YORK POLYCLINIC,

AND E. E. SMITH, PH. D.

It is the aim of this paper to present the results of a research upon epilepsy that has been in progress during the past winter. This research was originally undertaken with a view to studying the relation of uric-acid excretion to the epileptic paroxysm—a line of inquiry brought to our notice by the recent publications of an English writer, Haig.† According to this author, the *grand mal* seizure is determined by an excessive accumulation of uric acid in the blood. In the study of this question our results were not confirmatory of the view of Haig. Certain observations, however, of another kind, suggested to us the possibility of a causal relationship in some cases between putrefactive processes in the intestine and epileptic seizures. As a consequence we were led to undertake the research that

* Read before the American Neurological Association.

† *Uric Acid as a Factor in the Causation of Disease*, 1892.



is here recorded and with which the greater part of this paper is concerned. Evidently the planning of a study of this character involves the assumption that the discharge of nerve force from the cortex which constitutes the epileptic seizure may be in some way conditioned by the quality of the blood by which the cerebral elements are nourished. The idea that epileptic paroxysms may be related to toxic substances in the blood is not a new one, the clinical aspects of epilepsy being such that they have suggested a dependence of this kind to some authors who have not been satisfied with the purely mechanical explanation of the epileptic seizure. Thus Flint * says: "In a large proportion of the cases of epilepsy no sources of centric or of eccentric irritation are apparent. That under these circumstances the epileptic paroxysms are due to the action of an internal and at present unknown toxical agent seems to me the most rational hypothesis." That toxic substances produced in the intestine may sometimes determine the occurrence of epileptic seizures is a possibility that occurs to one on considering the cases of epilepsy in which the symptoms of disordered digestion, often from an error in diet, are associated with an unusual frequency of the seizures. The observations which we have made upon intestinal putrefactive processes in epileptics are based upon a study of the urine of such cases. As we shall explain further on at greater length, certain substances in the urine—namely, the ethereal sulphates—have been shown to be derived from putrefaction in the intestine, and the extent to which such putrefaction occurs may be inferred, bearing in mind certain precautions, from the quantity of these substances in the urine. These substances have been studied by us in thirty-one different cases of epilepsy, most of the cases being unquestionably idiopathic in nature, according to the generally accepted meaning of this

* *Practice of Medicine*. Sixth edition, p. 825.

term. In the majority of these cases the uric-acid excretion also has been studied. The results that have been derived from this inquiry may be presented under the following titles :

First. Synopses of the clinical histories of the cases of epilepsy that form the basis of this paper, together with the tabulated results obtained from analysis of the urine.

Second. Conclusions relating to the excretion of uric acid in epilepsy.

Third. Conclusions relating to the occurrence of intestinal putrefaction in epilepsy.

CASE I.—J. V. S., aged fifty-two ; weight, one hundred and seventy pounds. First *grand mal* seizure occurred during night in patient's forty-third year. Consisted of a general convulsion without aura, biting of tongue, or passage of urine, followed by active delirium and deep sleep. *Grand mal* seizures increased gradually in frequency ; they now recur three or four times a month. Two years after first seizure developed *petit mal* attacks, of which there are several a week. Slight loss of mental power. General health fair. Has always been predisposed to diarrhœa and dyspepsia.

CASE II.—M. R., female, aged twenty-four ; weight, one hundred pounds. Has had typical *grand mal* paroxysms for four years, two to three every month. No known cause. Paroxysms have been diminished in frequency (one to two months) under bromide treatment. Seizures usually occur just before, during, or after menstrual period. General health feeble. Marked anæmia. Intercostal neuralgia. Frequent attacks of gastric pain after food. Occasional constipation.

CASE III.—M. M., aged twenty-six. *Grand mal* seizures for several years. Developed without known cause. At first had only three or four seizures a year ; now has about one a month, usually during or just after menstrual period. Epigastric aura. Bites tongue. Clonic spasm general. Seizure followed by stupor. No appreciable mental impairment. General health good. Digestion usually good. Seldom constipated.

CASE IV.—E. E., aged twenty-six; weight, one hundred and sixty (?) pounds. Good health until two years ago. At the time was struck upon the right side of the head by the falling of a brick. No loss of consciousness resulted, but a scalp wound was made. About two months later had the first epileptic seizure. Since that time there have been many seizures, and at the present time there are many seizures weekly. Frequently there are many seizures in succession. The convulsions are general. Much mental impairment. General health good. No constipation or digestive disorder.

CASE V.—C. C. P., male, aged sixteen; weight, one hundred and thirty-five pounds. Epileptic convulsions since third year. Early history obscure. Paroxysms said to have come on without cause. Much mental impairment. Seizures two to four a week; uncontrolled by bromides. No aura. Deviation of eyes to right; clonic spasm more marked on right side. General health excellent. No evidences of indigestion. No constipation. Suspicion that the disease may have been of organic origin.

CASE VI.—C. T. B., male, aged thirty-four; weight, one hundred and fifty pounds. Seizures commenced during early childhood without known cause. Have continued without change in frequency or character. Much mental impairment. Seizures, five or six a month; uncontrolled by bromides. Typical *grand mal* seizures. Clonic spasm general. Sensory aura in small proportion of seizures (one in ten). General health robust.

CASE VII.—F. G. S., aged thirty. First *grand mal* seizure at age of ten (without known cause?). Now has two or three seizures a month. Often these are followed by maniacal excitement. General health good. Great mental enfeeblement. Is apt to become constipated. Two months ago became constipated, and the *grand mal* seizures became more frequent and severe during this time than usual. Does not suffer from dyspepsia.

CASE VIII.—E. M. B., aged fifty. For more than twenty years has had infrequent typical *grand mal* seizures, which developed without known cause. Considerable mental excitement before and after seizures. Has been free from seizures as long

as three years. At present has two or three seizures every fortnight. Great mental enfeeblement. General health excellent. Does not suffer from dyspepsia or constipation. Has a uterine fibroid. This began to grow rapidly five years ago, and the seizures have been more frequent ever since.

CASE IX.—P. S., male, aged sixty-three; weight, one hundred and sixty pounds. One uncle epileptic. Rugged health until eighteen years ago. Then a sudden mental shock was followed by first *petit mal* seizure. *Petit mal* seizures increased gradually in frequency from one a month to five a day in 1888. Then first *grand mal* seizure. *Grand mal* seizures of typical character at night; loss of consciousness, with falling, but without true convulsive movements, during day. Falling seizures about one a day. On bromides since first *petit mal* seizure. Seizures much more frequent when bromides discontinued. Gastric dyspepsia since bromides begun. Transient glycosuria at times. General health excellent. Very little mental impairment. Bowels regular usually.

CASE X.—S. S., aged twenty-nine; weight, one hundred and fifteen (?) pounds. First epileptic seizure occurred at age of eighteen, without known cause. The first seizure coincided with the menstrual period. Since then seizures have been frequent. Several typical *grand mal* seizures occur at present in the course of a week. Patient has a vague epigastric aura. Always cries out. Has occasional *petit mal* seizures. Mental condition good. General health good. Bowels regular.

CASE XI.—E. B., aged forty-five; weight, one hundred and forty (?) pounds. Patient had the first *grand mal* seizure fifteen years ago. Came on without known cause. Received a severe burn of the right hand in the first seizure. Has had ever since many *grand mal* seizures monthly, and usually several *petit mal* seizures. No relation of the seizures to menstruation. During past year seizures have been somewhat less frequent than formerly. Little or no mental impairment. General health excellent. Neither indigestion nor constipation.

CASE XII.—K. S., aged forty-three; weight, one hundred and ten pounds. First seizure at age of seventeen, without known cause. Now has about one seizure a week, and several *petit*

mal seizures daily. No aura. No relation of *grand mal* to menstrual periods. Much mental impairment. General health fair. Is not dyspeptic.

CASE XIII.—K. M., aged twenty-four; weight, one hundred and sixty (?) pounds. Has had typical *grand mal* seizures since her eleventh year. These came on without known cause. Seizures were very frequent from the beginning (several a week). At present patient is having from six to twelve seizures daily. Often one seizure occurs directly after another. Both clonic and tonic spasm are usually rather more marked upon the right side. Stupor lasts long after seizures. Great mental impairment and continuous dullness. No relation of seizures to menstruation. General nutrition good.

CASE XIV.—B. F., aged nineteen. First *grand mal* seizure at the age of ten without known cause. Seizures frequent from the first. Menstruation at thirteen. Seizures especially frequent about menstrual period. Now has several seizures daily (three to five), sometimes as many as twelve. No distinct aura. Patient utters a cry and falls. A short period of general rigidity is followed by clonic spasm, chiefly of left arm. After this, patient grows violent and abusive for a short time. Seizures vary much in severity and duration. Mental power not greatly impaired. General health good. Chronic constipation.

CASE XV.—K. A., aged twenty-five. First *grand mal* seizure at age of thirteen, without known cause. First menstrual period about a month after first seizure. Seizures from two to twelve a month; severe and typical *grand mal*. More frequent at menstrual period; less frequent now than formerly. Considerable mental impairment. General health good. Usually constipated.

CASE XVI.—S. C., aged thirty-one; weight, one hundred and twenty-five pounds. First *grand mal* seizure at fifteen, without known cause. Seizures increased gradually in frequency; now has eight to ten seizures a month. Seizures are rather more frequent about the menstrual period. General health good, with the exception that patient suffers from dysmenorrhœa. Slight mental failure. Is not troubled with constipation or indigestion.

CASE XVII.—K. M., aged twenty-two; weight, one hundred and thirty (?) pounds. Has had *grand mal* seizures since her thirteenth year. Seizures average one or two a month. They usually occur just before or during a menstrual period. No aura. No *petit mal* seizures. Mental condition apparently little impaired. General health excellent. Is usually constipated.

CASE XVIII.—M. D., aged thirty-five; weight, one hundred and thirty pounds. First *grand mal* seizure in seventeenth year, without known cause. At one time had ten to twelve seizures a month; now has about seven seizures a month. Seizures are a little more frequent at menstrual periods. Has two or three *petit mal* seizures a month. General health good. Considerable mental failure. Is not troubled with constipation or indigestion.

CASE XIX.—R. M., aged seventeen. First *grand mal* seizure at age of thirteen, without known cause. Seizures have been frequent ever since this time, and now occur from three to five times a week. Menstruation began at the age of fourteen, and has always been scanty and irregular. Now suffers from amenorrhœa. Mental condition good. General health good. Does not suffer from indigestion or constipation.

CASE XX.—M. J., aged thirty-three; weight, about one hundred and forty pounds. First seizure occurred during eleventh year without known cause. Since then has had many *grand mal* seizures monthly until recently. Has had as many as sixteen seizures a day; now has one or two in the month. General health good. Intelligence somewhat impaired. Is troubled with constipation, but seldom has indigestion.

CASE XXI.—D. K., aged thirty-seven; weight, about one hundred and thirty pounds. At age of fourteen had the first *grand mal* seizure, which came on without known cause. Since that time has been having from six to ten severe *grand mal* seizures, with prolonged loss of consciousness, in the month. Seizures are rather less frequent now than formerly. They occur with especial frequency at the beginning of the menstrual period. Is much troubled with constipation. Is not troubled with indigestion.

CASE XXI.—A. W., female, aged thirty-seven. *Grand mal* seizures since age of thirteen. First seizure occurred about time of first menstruation, but referred to fright. Four or five paroxysms monthly, three or four of them usually within a few days of period. Considerable mental impairment. General health good. No digestive disorders. No constipation. Bromide treatment.

CASE XXIII.—F. K., female, aged thirty-four. Seizures commenced at the age of eighteen without known cause. Has both *grand* and *petit mal* paroxysms, the former especially at the menstrual period. Three to four *grand mal* seizures a month. Three to five *petit mal* seizures a week. *Grand mal* seizures formerly more frequent than now; appear to be partly controlled by bromides. General health good. Does not suffer from indigestion or constipation.

CASE XXIV.—A. D., female, aged thirty-nine; weight, one hundred and eighty (?) pounds. Severe typical *grand mal* seizures began nine years ago at a time of grief and anxiety. Seizures especially apt to occur at menstrual period; three or four a month; formerly one or two a month. (Constipation and indigestion marked.) Mental state good. General health robust. No bromides for five months.

CASE XXV.—B., female, aged thirty-one. *Grand mal* paroxysms began twelve years ago without known cause. Three or four seizures a month; formerly less frequent. Seizures especially apt to occur during the week after menstruation. Mental condition good. General health robust. Suffers from constipation and indigestion.

CASE XXVI.—M. H., aged thirty; weight, one hundred and ten pounds. Seizures of typical *grand mal* coming about three years before without known cause. Second seizure about one year after first; third, about six months after second. Now has one seizure about every month. Non-menstrual. Aura and cry before seizure. Tonic followed by general clonic convulsions. Mental condition good. General health good. Does not suffer from constipation or indigestion. Severe bromism at one time.

CASE XXVII.—Julia Hackett, aged fifty-nine; weight, one

hundred and sixty-five (?) pounds. Severe and typical *grand mal* seizures since her ninth year. First seizure occurred about two weeks after a fright received from falling from an apple tree. Slight scalp wound at this time. Has about one seizure a month at present; formerly had several a month. No aura. Onset of seizures very sudden. Period of tonic spasm very short; spasm clonic almost from first. Duration, two to three minutes. Mental condition apparently unimpaired. General health robust. Bowels regular. No symptoms of dyspepsia.

CASE XXVIII.—M. R., aged twenty-four; weight, one hundred and ten (?) pounds. Severe *grand mal* seizures began at age of five, without known cause, but early history is obscure. During past four years has had from five to ten severe *grand mal* seizures a month. Especially frequent just before or during menstrual period. No aura; screams and falls suddenly; long period of rigidity (two minutes) before general clonic spasm comes on. Great mental enfeeblement. General health good. Appetite good. Frequent constipation. No dyspeptic symptoms.

CASE XXIX.—D. H., aged twenty-seven; weight, one hundred and three pounds. When seven years of age began to have *petit mal* seizures, which developed without known cause. Seizures continued for several years, ceased spontaneously, and then recurred. Has from three to ten seizures a week. Usually a painful epigastric aura an appreciable time before the seizure, which consists of temporary loss of consciousness, during which there are automatic movements. After seizure, patient is pugnacious. Seizures diminished in frequency under influence of bromides. Slight mental weakness. General health fair.

CASE XXX.—R. K., female, aged thirty-six; weight, ninety-nine pounds. Good health until twelfth year. Then first *petit mal* seizure without apparent cause. Several *petit mal* seizures daily. Aura of general painful sensation all over her, with accumulation of gas in intestines, arrested by inhaling amyl nitrite. Great increase of attacks on removal of bromides. Seizures most frequent at menstrual period. Rarely *grand mal* seizure. General health fair; suffers from constipation.

CASE XXXI.—J. K. S., aged thirty-three; weight, one hundred and thirty-eight pounds. Was in good health until two years ago, when he had a slight *petit mal* seizure; sudden loss of consciousness, with pallor, while in sitting posture and talking. Duration of first seizure, a few seconds only. Second seizure, six months after first and slight. Since then seizures much more frequent and more severe. Loss of consciousness and pallor, followed by temporary mental confusion. One hundred and fifty-one seizures in first three months of 1892. Mental power considerably impaired. General health good. Bowels regular.

SYNOPSIS OF THE CLINICAL HISTORIES, TOGETHER WITH THE
TABULATED RESULTS OBTAINED FROM ANALYSIS OF THE
URINE.

In selecting the foregoing cases for study an effort was made to include only cases of idiopathic epilepsy. In three of the cases (IV, V, and VI) there is, however, reason to believe that the seizures may have been dependent on organic disease. In two of these three cases the seizures date from early childhood; in the other case they date from a severe injury to one side of the head.

Of the thirty-two cases of epilepsy, *grand mal* seizures were the distinctive features in twenty-nine. In the three remaining cases (XXIX, XXX, and XXXI) there were very frequent *petit mal* seizures. In one of these three cases there was no history of the occurrence of any *grand mal* paroxysms, but in the two others such paroxysms were said to occur at irregular and usually long intervals.

Eighteen of the thirty-one patients were inmates of the Hospital for Nervous Diseases, and we are indebted to Dr. E. D. Fisher and Dr. Frederick Peterson for their courtesy in placing these patients at our disposal for study.

Table showing the Excretion of Uric Acid and Urea and of the Sulphates and Indigo-Blue.

CASE AND DATE.	Volume.	Specific gravity.	Urea.	Uric acid.	Ratio of uric acid and urea.	Preformed sulphates.	Combined sulphates.	Ratio of preformed and combined sulphates.	Ratio of total sulphates and urea.	Indigo-blue.	REMARKS.
CASE I.											
October 26, 1891.....	C. c. 2,170	1·013½	Grammes. 21·49	Grammes. 0·590	36·4	Grammes.	Grammes. 0·0411	
" 28.....	1,780	1·015	22·59	0·520	43·4	
" 30.....	1,230	1·017½	19·51	(Lost.)	0·0458	
November 2.....	1,580	1·015	19·64	0·422	46·5	Grand mal seizure, night, November 2.
" 4.....	1,650	1·011½	19·98	Begins use of highly nitrogenous food.
" 6.....	1,500	1·019	28·70	0·666	43·1	
" 9.....	2,100	1·014	29·07	0·643	45·2	
" 11.....	1,320	1·012½	19·79	0·375	52·8	
" 13.....	1,650	1·015½	29·35	0·553	53·0	
" 19.....	1,425	1·023	37·26	(Lost.)	0·0344	
" 20.....	1,420	1·023	39·73	0·637	63·9	0·0552	Seizure at 3 A. M.
" 21.....	1,525	1·020½	41·20	0·534	77·1	0·0615	
" 22.....	1,690	1·020½	39·16	0·358	109·3	0·0824	
" 23.....	1,555	1·022	38·12	0·686	55·5	0·0636	
" 24.....	1,750	1·020	41·39	0·749	55·2	0·0516	
" 25.....	1,535?	1·019½	36·60	0·648	56·4	0·0517	
December 6.....	2,190	1·013	27·79	0·627	44·3	0·167	13·0	11·6	From December 1-8, 15 grammes sodium salicylate t. i. d.
" 7.....	2,300?	1·014½	29·19	0·554	52·7	
" 8.....	1,860	1·016	24·14	0·379	63·7	

CASE AND DATE.	Volume.	Specific gravity.	Urea.	Uric acid.	Ratio of uric acid and urea.	Preformed sulphates.	Combined sulphates.	Ratio of preformed and combined sulphates.	Ratio of total sulphates and urea.	Indigo-blue.	REMARKS.
	C. c.		Grammes.	Grammes.		Grammes.	Grammes.			Grammes.	
December 9.....	2,120	1.014	23.03	0.367	66.3	1.745	0.237	7.5	11.6	0.009	
" 10.....	1,550	1.017 $\frac{1}{2}$	24.29	0.462	52.5	
" 11.....	1,560	1.021	26.54	0.513	51.7	
" 27.....	1,380	1.017 $\frac{1}{2}$	25.08	0.400	62.7	1.740	0.285	6.1	12.2	0.0392	
" 28.....	2,115	1.014	23.15	0.506	38.8	1.695	0.225	7.3	12.4	0.0171	Blurred vision to-day.
" 29.....	1,945	1.016 $\frac{1}{2}$	24.90	0.486	51.2	1.915	0.235	8.1	11.1	0.0318	
" 30.....	1,315	1.017	22.36	0.379	59.2	1.780	0.087	20.4	11.9	0.0163	
" 31.....	1,505	1.015 $\frac{1}{2}$	26.47	0.408	64.9	1.964	0.173	11.3	12.4	0.0312	
January 1, 1892.....	1,610	1.019 $\frac{1}{2}$	31.15	0.557	55.9	2.077	0.262	7.9	13.3	0.0573	Ate and smoked to excess to-day.
" 2, I.....	845	1.017	14.78	0.258	57.2	Mild seizure at 7.30 A. M., January 2.
" 2, II.....	435.9	1.016 $\frac{1}{2}$	5.65	0.096	58.8	
" 2, III.....	735	1.009 $\frac{1}{2}$	5.24	0.103	50.9	
" 2 (total).....	2,015	25.68	0.437	56.1	2.045	0.318	6.4	0.0453	
" 3.....	1,175	1.019	21.47	0.467	46.0	1.698	0.281	7.3	0.032	
" 4.....	1,925	1.015	23.39	0.429	59.2	1.505	0.383	3.9	0.039	
" 5.....	1,400	1.020	21.34	0.426	50.1	1.765	0.256	6.9	0.0379	
" 21.....	1,460	1.015	26.11	0.500	52.2	1.437	0.533	2.7	0.569	
" 23, II.....	705	1.015	5.44	0.172	31.6	
" 23, III.....	335	1.012	8.64	0.143	60.4	
" 23, II, III.....	1,040	14.08	0.315	44.7	0.772	0.124	4.4	
" 24.....	1,185	1.013 $\frac{1}{2}$	15.63	0.586	26.6	1.337	0.174	7.6	0.0207	

January 31.....	1,540	29.87	0.764	39.1	2.428	0.331	7.3	0.0564
February 1.....	1,270	19.68	0.441	44.6	1.800	0.208	65.0
" 2.....	1,390	20.85	0.401	50.0	1.638	0.223	7.0
" 3, I.....	1,070	19.58	0.426	45.9
" 3, II.....	320	4.60	0.085	53.8
" 3, III.....	520	6.39	0.169	37.8
" 3 (total)....	1,910	30.58	0.680	44.9	3.415	0.373	9.1	0.0695
" 4.....	1,090	23.87	0.563	42.4	2.034	0.194	10.3
" 5.....	1,455	26.33	0.604	43.6	2.175	0.216	10.0
" 8, 9.....	1,420 1,520	3.597	0.507	7.0	0.0697
" 10.....	1,365	1.928	0.275	7.0
March 10, I.....	825	14.93	0.212	70.4
" 10, II.....	780	12.55	0.481	26.1
" 10 (total)....	1,605	27.49	0.693	39.6
" 31.....	1,820	34.94	0.545	61.1	4.022	0.237	17.0	Milk diet commenc'd.
April 27.....	1,635	33.49	0.561	59.7	2.77	0.232	11.0
" 27, 28, I.....	850	8.92	0.136	65.6	0.717	0.052	13.8
" 27, 28, II.....	530	7.82	0.110	71.1	0.493	0.046	10.7
" 27, 28, III.....	610	7.61	0.176	43.2	0.521	0.050	10.4
" 27, 28, I, II, III.	1,990	24.36	0.422	57.7	1.730	0.149	11.6
" 28, 29.....	1,670	30.39	0.518	58.6	2.439	0.226	10.8
May 6.....	1,855	30.48	0.528	57.7	2.306	0.217	10.6	Almost negative.
" 9.....	1,715	24.07	0.419	57.4	Strong.
" 10, I.....	1,520	20.07	0.364	55.1	Strong.
" 10, II.....	225	3.32	0.054	61.0	Seizure at 7.45 A. M.
" 10, III.....	705	7.40	0.223	33.2	Ate asparagus on night of May 9.
" 10, I, II, III.....	2,450	30.80	0.679	45.2

CASE AND DATE.	Volume.	Specific gravity.	Urea.	Uric acid.		Ratio of uric acid and urea.	Preformed sulphates.		Combined sulphates.	Ratio of preformed and combined sulphates.	Indigo-blue.	REMARKS.
				Grammes.	Grammes.		Grammes.	Grammes.				
May 11.....	C. c. 1,250	1·013	19·24	0·402	47·8	Grammes.	Seizure at 6.30 A. M., May 16.
" 14, 15.....	1,980	1·011	26·56	0·464	57·2	
" 15, I.....	1,080	1·011	11·90	0·203	58·6	
" 15, II.....	570	1·015	8·18	0·143	57·2	
" 15, III.....	320	1·021	6·98	0·215	32·5	
" 15, I, II, III.....	1,970	27·07	0·561	48·2	
" 16, 17.....	700	1·018	16·38	0·340	48·1	
June 4.....	1,440	1·010	15·64	1·178	0·254	4·6	Medium strong.	
CASE II.												
October 8, 1891.....	920	1·014	9·377	0·339	23·4	One seizure. 24 hours following seizure.
" 20.....	1,340	1·011	13·780	0·440	31·3	0·0095	
" 20.....	196	1·019	0·135	
" 27.....	1,160	1·016	16·955	0·529	32·0	Traces.	
November 2.....	1,200	1·019½	22·155	0·635	34·9	
December 29.....	590	1·021½	20·529	0·639	32·1	Traces only.	
January 5, 1892.....	530	1·019	9·064	0·380	23·8	0·525	0·162	3·2	
" 12.....	1,005	1·020	24·360	0·532	45·8	1·387	0·233	4·9	0·0113	
" 15.....	340	1·029½	12·295	0·321	38·3	0·839	0·108	7·8	
" 18.....	800	1·025½	23·142	0·565	40·9	1·381	0·206	6·7	Traces only.	
" 25.....	995	1·012½	12·390	0·375	32·9	0·679	0·191	3·5	0·0136	Two seizures on June 30.
" 28.....	2,095	1·014½	31·120	0·806	38·6	2·019	0·393	5·1	0·0158	

February 15.....	765	1·023½	1·312	0·136	8·6	One seizure.
March 5.....	835	1·026	2·263	0·273	8·2	
“ 19.....	1,910	1·018	2·086	0·221	6·5	
CASE III.									
November 12, 1891...	745	1·022	16·69	
January 29, 1892.....	705	1·009	6·95	0·228	0·079	4·1	
March 30.....	825	1·022	1·270	0·185	6·8	
CASE IV.									
February 4, 1892.....	900	1·021	24·12	0·386	62·4	0·229	After five <i>grand mal</i> seizures. Two seizures.
“ 4.....	820	1·016	19·27	0·329	58·5	
“ 5.....	815	1·023	26·97	0·456	59·1	
“ 5.....	1,635	46·24	0·785	58·9	0·212	One seizure.
“ 6.....	1,195	1·014	16·01	0·255	62·8	
“ 6, 7.....	990	1·018	19·00	0·231	82·2	
“ 6, 7.....	2,185	35·02	0·486	72·0	1·683	12·1	
“ 9, 10.....	1,020	1·026	34·37	0·442	77·7	0·139	
“ 15.....	1,013	0·985	0·088	15·8	
CASE V.									
February 9, 10, 1892...	690	1·024	17·319	0·451	38·4	9·085	10·4	Traces only.	12 hours following seizure.
“ 10, 11.....	400	1·026	14·360	0·388	37·0	
“ 11, 12.....	635	1·025	19·749	0·474	41·6	
“ 14, 15.....	590	1·027	26·373	0·419	62·9	Seizure between I and II.
“ 15, I.....	330	1·029	15·972	0·273	50·5	
“ 15, 16, II.....	260	1·025	10·140	0·176	56·6	0·422	8·9	Traces only.	
“ 15, 16, I, II.....	590	26·112	0·449	58·1	
“ 16, 17.....	520	1·027	22·360	0·476	47·0	
“ 20, 21.....	770	1·023	19·481	0·446	43·6	
“ 21, 22.....	660	1·023	18·216	0·448	40·6	5·729	13·3	0·0080	
“ 22, 23.....	630	1·025	20·160	0·648	31·1	0·431	

CASE AND DATE.	Volume.	Specific gravity.	Urea.	Uric acid.	Ratio of uric acid and urea.	Preformed sulphates.	Combined sulphates.	Ratio of preformed and combined sulphates.	Indigo-blue.	REMARKS.
CASE VI.										
February, 1892.....	C. c.		Grammes.	Grammes.		Grammes.	Grammes.		Grammes.	
I.....	785	1·019	25·512	0·439	58·1	
II.....	265	1·019	9·805	0·135	72·6	
	165	1·028	6·501	0·150	43·3	3·493	0·436	8·0	Traces only.	
I, II.....	430	16·306	0·285	57·1	Seizure between I and II.
.....	390	1·027	16·497	0·304	54·2	
February 29.....	925	1·025	27·935	0·768	36·3	
March 1, 2, I.....	375	1·012	7·65	0·144	53·1	
“ 2, II.....	310	1·023	10·57	0·220	48·0	5·590	0·798	7·0	0·0018	Seizure between I and II.
“ 2, I, II.....	685	18·22	0·364	50·0	
“ 2, 3.....	835	1·025	26·14	0·631	41·4	
CASE VII.										
February 15, 1892.....	875	1·020	19·16	0·348	55·0	
“ 16.....	1,425	1·023	35·48	0·769	46·1	5·278	0·524	10·0	One grand mal seizure.
“ 17.....	545	1·027	19·78	0·578	34·2	
“ 26.....	2,070	1·022	47·40	1·002	47·3	3·920	0·310	12·6	
“ 26.....	2,115	1·014	36·37	0·852	42·7	3·059	0·281	10·8	One grand mal seizure.
“ 26.....	2,080	1·018	38·68	0·733	52·7	2·938	0·383	7·7	
CASE VIII.										
February 22, 1892.....	660	1·023	17·88	0·443	40·3	2·470	0·311	7·9	One grand mal seizure.
“ 23.....	985	1·013	18·71	0·570	32·8	

(CASE IX.

March 13, 1892..... 900
 " 14..... 950
 May 24, 25..... 1,245
 " 26, 26..... 840
 " 26, 27..... 1,360

(CASE X.

March 9, 1892..... 1,160
 " 10..... 1,975
 " 11..... 835
 " 12..... 1,305
 " 13..... 825
 " 14..... 1,040
 " 15..... 1,140
 " 16..... 755
 " 17..... 1,700

May 19, 20..... 1,150
 " 20, 21..... 1,470
 " 21, 22..... 1,250
 " 22, 23..... 1,090
 " 23, 24..... 1,075
 " 24, 25..... 1,610
 " 25, 26..... 1,455

51.1 }
 45.4 }

1.015 10.53
 1.015 11.30
 1.015 16.710
 1.024 17.170
 1.020 22.843

0.206
 0.249

1.714
 1.415
 1.567
 1.763

0.332
 0.260
 0.198
 0.375

5.1
 5.4
 7.9
 4.7

....

9.8

0.241

2.375

0.504

25.40

1.160

7.1
 9.3

0.231
 0.211

1.652
 1.984

 4.614

0.311
 0.392
 0.220
 0.494
 0.337
 0.328
 0.281
 0.399

22.31
 22.54
 15.00
 23.01
 17.78
 18.01
 19.63
 20.40

1.975
 835
 1,305
 825
 1,040
 1,140
 755
 1,700

6.7

0.432

2.893

0.281
 0.399

28.61
 17.86
 31.50
 22.45
 26.24
 18.61
 24.63

1,150
 1,470
 1,250
 1,090
 1,075
 1,610
 1,455

15.3
 8.8
 9.6
 7.4
 7.8
 5.3
 7.3

0.242
 0.183
 0.306
 0.231
 0.217
 0.248
 0.251

3.711
 1.615
 2.962
 1.703
 1.706
 1.330
 1.847

.....

28.61
 17.86
 31.50
 22.45
 26.24
 18.61
 24.63

1,150
 1,470
 1,250
 1,090
 1,075
 1,610
 1,455

Sample of 24 hours' urine.

One *grand mal* seizure at night.

One *grand mal* seizure.

One seizure; sod. sal., gr. x, t.i.d.

"

"

"

Two seizures.

Sod. sal., gr. x, t. i. d.

CASE AND DATE.	Volume.	Specific gravity.	Urea.	Uric acid.	Ratio of uric acid and urea.	Preformed sulphates.	Combined sulphates.	Ratio of preformed and combined sulphates.	Indigo-blue.	REMARKS.
CASE XI.										
March 10, 1892.....	C. c. 1,225	1·012	Grammes, 15·80	Grammes, 0·387	40·8	Grammes, 1·134	Grammes, 0·265	4·2	Grammes,	
" 12.....	1,525	1·014	22·41	0·482	46·5	2·537	0·508	5·0	
" 13.....	920	1·014	14·44	0·292	49·4	1·850	0·363	5·1	One <i>grand mal</i> seizure.
" 14.....	1,960	1·014	25·48	0·625	40·7	3·227	0·549	5·8	One <i>grand mal</i> seizure.
" 15.....	910	1·018	18·38	0·353	52·0	1·063	0·188	5·6	One <i>grand mal</i> seizure.
" 16.....	840	1·019	22·09	0·370	59·7					
" 17.....	1,220	1·011	15·25	0·307	49·6					
CASE XII.										
March 22, 23, 1892...	990	1·013	15·93	0·192	83·0					
" 23, 24.....	780	1·013	14·74	0·230	64·0	3·344	0·536	6·2	
" 24, 25.....	585	1·019	16·16	0·228	70·8					
" 26, 27.....	580	1·017	16·41	0·209	78·5	1·090	0·165	6·6	
" 28, 29.....	1,550	1·015	27·43	0·273	100·4	2·143	0·251	8·3	One <i>grand mal</i> paroxysm.
CASE XIII.										
March 22, 23, 1892...	480	1·020	4·88	0·166	25·4	1·699	0·152	11·2	Eight seizures.
" 23, 24.....	210	1·015	1·688	0·072	23·2	Partial sample for 24 hours; nine seizures.
" 28, 29.....	770	1·010	7·909	0·116	68·1	1·559	0·179	8·7	{	Ten seizures.
" 30, 31.....	910	1·008	10·62	0·212	50·0					

CASE XIV.

March 29, 30, 1892...	1,800	1·009	20·34	0·263	77·3	2·411	0·516	4·7	{	Six seizures.
" 30, 31.....	2,035	1·007	14·24	0·394	36·1				{	Nine seizures.
" 31 to April 7...	1,900	1·011	26·03	0·550	47·3	4·364	0·505	8·6	{	Twelve seizures.
April 1, 2.....	1,720	1·015	31·30	0·495	65·0				{	Seven seizures.
May 19, 20.....	1,560	1·013	19·92	1·500	0·243	6·2	Four seiz.; sod. sal., gr. xv, t.i.d.
" 20, 21.....	2,000	1·012	25·95	2·203	0·233	9·4	Three " " "
" 21, 22.....	1,460	1·012	25·06	1·904	0·219	8·7	Four " " "
" 22, 23.....	785	1·014	15·22	1·060	0·144	7·3	Three " " "
" 23, 24.....	1,555	1·009	19·72	1·572	0·140	11·2	Three " " "
" 25, 26.....	1,530	1·012	25·69	2·008	0·293	6·8	Six " " "
June 2, 3.....	1,870	1·009	22·82	1·746	0·343	5·1	Sod. bicar., gr. xx, t.i.d.
" 3, 4.....	1,830	1·007	8·54	0·648	0·272	2·4	Three " " "
" 4, 5.....	1,845	1·008	9·95	0·866	0·237	3·6	" " "
" 5, 6.....	1,840	1·011	17·05	1·097	0·333	3·3	Three " " "
" 6, 7.....	1,675	1·007	15·68	0·895	0·293	3·0	Four " " "
" 7, 8.....	1,770	1·005	11·91	0·721	0·241	3·0	Two " " "
" 8, 9.....	1,060	1·003	5·20	0·284	0·106	2·7	Three " " "
" 10, 11.....	1,475	1·009	12·62	0·895	0·303	2·9	Three seizures.
" 11, 12.....	1,980	1·015	11·88	0·873	0·205	4·2	Four seizures.
" 12, 13.....	1,780	1·008	20·71	1·458	0·310	4·7	Three seizures.

CASE XV.

April 2-4, 1892.....	3,825	1·002	12·34	1·024	0·147	7·0	
" 4, 5.....	1,960	1·004	11·97	0·328	36·4	2·253	0·386	5·8	One seizure.
" 5, 6.....	2,065	1·007	16·89	0·374	45·1					

CASE XVIII.

May 6, 7.....	1,505	1·012	22·85	0·349	65·5	1·519	0·221	6·7	One seizure. One seizure, May 10, 11.
" 8, 9.....	1,965	1·006	18·69	0·398	47·0	1·316	0·139	9·4	
" 9, 10.....	1,400	1·005	13·10	0·924	0·198	4·6	

CASE XIX.

May 8, 9.....	1,710	1·008	17·78	1·296	0·151	8·5	Two seizures.
" 9, 10.....	1,835	1·011	21·56	1·701	0·208	8·4	
" 10, 11.....	1,815	1·007	18·02	1·535	0·162	9·4	

CASE XX.

May 12, 13.....	1,515	1·011	32·81	1·961	0·148	13·2	One seizure.
" 13, 14.....	2,025	1·010	28·44	1·599	0·165	9·6	
" 15, 16.....	1,485	1·015	2·434	0·272	9·1	

CASE XXI.

May 14, 15.....	1,155	1·013	24·08	1·507	0·254	5·9	One seizure.
" 15, 16.....	940	1·015	19·64	1·351	0·240	5·6	
" 16, 17.....	1,285	1·014	20·35	1·806	0·227	7·9	

CASE XXII.

May 17, 18.....	1,480	1·008	9·64	0·812	0·082	9·9	One slight seizure.
" 18, 19.....	1,730	1·006	8·61	0·649	0·109	5·9	
" 19, 20.....	1,800	1·005	10·86	0·777	0·108	6·5	

CASE XXIII.

May 20, 21.....	1,780	1·009	15·90	1·350	0·204	6·6	One seizure.
" 21, 22.....	1,350	1·012	14·32	1·135	0·170	6·6	
" 22, 23.....	1,050	1·013	13·26	0·993	0·146	6·8	

CASE AND DATE.	Volume.	Specific gravity.	Urea.	Uric acid.	Ratio of uric acid and urea.	Preformed sulphates.	Combined sulphates.	Ratio of preformed and combined sulphates.	Indigo-blue.	REMARKS.
	C. c.		Grammes.	Grammes.		Grammes.	Grammes.		Grammes.	
CASE XXIV.										
May 27, 28.....	1,620	1·012	19·88	1·723	0·262	6·6	
" 28, 29.....	1,735	1·013	22·85	2·018	0·460	4·4	One severe seizure.
" 29, 30.....	1,235	1·013	25·05	1·884	0·165	11·4	
CASE XXV.										
May 30, 31.....	1,520	1·014	27·25	2·102	0·224	9·3	One seizure.
May 31 to June 1....	1,440	1·013	21·48	1·666	0·199	8·3	
June 2, 3.....	1,045	1·016	25·20	1·955	0·215	9·0	Sod. bicarb., gr. xx, t. i. d.
" 3, 4.....	1,595	1·011	17·52	1·573	0·213	7·4	"
" 4, 5.....	1,620	1·013	19·44	1·640	0·204	8·0	"
" 5, 6.....	1,725	1·016	28·67	2·442	0·248	9·8	"
" 6, 7.....	1,110	1·018	23·68	1·930	0·231	8·3	"
" 7, 8.....	1,855	1·009	20·68	1·678	0·220	7·6	One seizure.
" 8, 9.....	2,030	1·003	31·87	2·443	0·275	8·9	"
" 10, 11.....	1,450	1·010	16·37	1·516	0·137	11·0	"
" 11, 12.....	835	1·022	20·67	1·955	0·212	9·2	One seizure.
" 12, 13.....	580	1·015	9·88	0·844	0·096	8·8	"
" 13, 14.....	565	1·024	18·80	1·639	0·163	10·5	
" 14, 15.....	1,080	1·020	25·40	2·077	0·201	10·3	

CASE XXVI.

June 1, 2,	520
" 2, 3,	510
" 3, 4,	620

CASE XXVII.

June 2, 3,	1,160
" 3, 4,	1,550
" 6, 7,	990
" 7, 8,	1,460
" 8, 9,	1,880
" 9, 10,	1,845
" 10, 11,	1,865
" 13, 14,	395
" 14, 15,	885

CASE XXVIII.

June 2, 3,	1,775
" 3, 4,	1,770
" 4, 5,	1,760

CASE XXIX.

December 29, 1891...	850
January 11, 1892....	1,290
" 17,	1,255
" 20,	155
" 20,	1,875
" 20,	2,030

34.2
.....	1.030	0.147	7.0
35.8	1.258	0.167	7.5
.....	Ethereal sulphates.	One seizure.
.....	1.473	0.344	4.2
.....	1.013	0.275	3.6
.....	1.490	0.280	5.3	One seizure.
.....	1.531	0.303	5.0
.....	1.230	0.226	5.4
.....	1.434	0.334	4.3	One seizure.
.....	1.026	0.361	2.8
.....	1.246	0.221	5.6
.....	1.880	0.306	6.1
.....	1.008	0.237	4.2
.....	0.996	0.192	5.0	One grand mal seizure to day.
.....	1.523	0.258	5.9
.....	Combined sulphates.
33.0	0.0044	Several petit mal seizures week-ly.
53.8	0.164	0.0164
60.3	2.876	0.200	13.7	Traces only.
.....
70.0
.....	2.456	0.234	10.5	Traces only.

CASE AND DATE.	Volume.	Specific gravity.	Urea.	Uric acid.	Ratio of uric acid and urea.	Preformed sulphates.	Combined sulphates.	Ratio of performed and combined sulphates.	Indigo-blue.	REMARKS.
	C. c.		Grammes.	Grammes.		Grammes.	Grammes.		Grammes.	
January 27.....	1,260	1·012	14·28	0·352	40·5	1·207	0·128	9·4	
" 28.....	134	1·019	2·69	0·048	56·2	
" 28.....	1,210	1·012	17·97	0·347	52·1	
" 28.....	1,344	20·67	0·395	52·3	1·632	0·207	7·9	Traces only.	
" 29.....	1,520	1·012	19·16	0·386	49·1	1·738	0·221	7·8	"	
" 30.....	910	1·012	14·58	0·238	61·2	
" 30.....	460	1·018	8·58	0·217	39·5	
" 30.....	1,370	23·17	0·455	50·9	2·081	0·184	11·3	Traces only.	
" 31.....	1,015	1·017	20·73	0·447	46·3	
" 31.....	400	1·013	5·35	0·123	43·5	
" 31.....	1,415	26·08	0·570	45·7	2·327	0·209	11·1	Traces only.	
February 2.....	2,040	1·014	29·17	0·706	41·3	2·643	0·261	10·1	"	
" 3.....	1,750	1·013	20·47	0·489	41·9	1·813	0·253	7·1	"	
" 10.....	1,345	1·013	20·71	0·460	45·0	2·202	0·109	20·2	
April 9.....	805	1·018	18·99	0·346	54·9	1·701	0·093	17·3	

CASE XXX.

March 3, 1892.....	600	1·020
" 4.....	830	1·020	0·478
" 4, 5.....	910	1·023	0·544	32·5	36·8
" 5, 6.....	890	1·023	0·526	39·2	43·2	4·867	0·238	20·4
" 6, 7.....	775	1·025	0·415	39·2
" 7, 8.....	830	1·023	0·419	39·2
" 9, 10.....	950	1·012	0·194	61·4
" 10, 11.....	945	1·012	0·226	66·1
" 11, 12.....	960	1·014	0·226	76·5
" 12, 13.....	990	1·012	0·204	85·8	2·751	0·110	25·0
May 4.....	1,680	1·021
" 5, 6.....	950	1·015
CASE XXXI.									
March 9, 1892.....	855	1·031	24·54	0·593	41·3	2·208	0·137	16·1
April 25.....	935	1·031	34·59	0·521	66·4	2·565	0·148	17·3

Conclusions relating to the Excretion of Uric Acid in Epilepsy.—Is the epileptic paroxysm associated with any peculiarities in the excretion of uric acid? According to Haig, there is a great diminution in uric-acid excretion before the paroxysm, and an equally considerable increase in the uric acid excreted at the time of the paroxysm. Looking at those of our figures that relate to the elimination of uric acid before the seizure, we find that the excretion has only in rare instances varied from the limits of health. This is true both of the cases where the urine just before the paroxysm was examined, and of the instances where only the urine for the twenty-four hours preceding the day of the seizure was studied.* In a few instances the uric-acid content has been higher than is seen in health, but this has been in cases where high uric acids were frequent without respect to the time of the seizures.† The general statement

* In studying the relation of uric-acid excretion to the epileptic seizure we have to look both at the results obtained from the estimation of uric acid in the twenty-four hours' urine immediately preceding, in that of, and in that immediately following the seizure, and at the results obtained from the estimation of uric acid in divided portions of the urine of the twenty-four hours in which the paroxysm has occurred. The latter method is followed in some instances because there is the possibility that abnormalities in separate portions may neutralize one another in the total twenty-four hours' urine and thus escape detection. For instance, the urine before the seizure might contain abnormally little uric acid, and that at the time of or after the seizure a large excess; but a mixture of the two portions might show no departure from the normal limits.

† One of the first things that one notices in looking over the tables is that in nearly every case some of the twenty-four hours' urines show deviations from the normal ratios (1:46 to 1:65). In sixteen of the twenty-one cases where uric acid was studied, the uric acid varies from the limits of health, most of them showing a considerable proportion of urines in which the ratio to urea is distinctly high. The same cases and some of the others show also a deviation of another character.

may safely be made that there is nothing distinctive about the uric-acid content of the urine just before a paroxysm. The urines passed on the days of paroxysms (total twenty-four hours) and the urine passed *immediately* after seizures have also shown nothing distinctive. The latter are apt to show a higher uric-acid ratio than the urines passed just before seizures; very often, however, the ratio is one that belongs within the limits observed in health.

In general, it may be said that the urine passed after a seizure is apt to have a higher uric-acid ratio than the urine before or about the time of the seizure (including that passed immediately after). The difficulty in getting the conditions in the collection of urine the same in different cases makes numerical comparisons difficult. Of fifteen seizures where a comparison may be made of the uric-acid content of the urines after seizures (either immediately or the day after) with the uric-acid content on the day of the seizures, the urines in nine cases showed an increase in the uric-acid content after the seizures, and in six of these cases the uric-acid ratio was higher than 1 to 45.* This tendency to a high uric-acid ratio after paroxysms is to be regarded as a consequence of conditions which determine the seizures, or possibly of the seizure itself. The excess of uric acid that is observed in epilepsy can not reasonably be construed as the cause of seizures.† The foregoing remarks apply to cases of *grand mal*. In *petit mal* cases we have observed a continuously high uric-acid excretion which appeared to be related in some way to the cause of the seizures. It was

While many of the ratios are such as are met with in health among different individuals, the variations are certainly wider from day to day than those of individuals in health and on a reasonably constant diet.

* These ratios are as follows: 50, 43, 38, 37, 31, 43, 48, 34, and 51.

† See also Herter and Smith. Observations on the Excretion of Uric Acid in Health and Disease. *N. Y. Medical Journal*, June 4, 1892.

found in two out of three *petit mal* cases that when the excretion of uric acid was reduced to normal by the use of a milk diet, the seizures were greatly reduced in frequency. This effect upon the seizures of reducing the uric-acid excretion has been of considerable duration in these cases and may prove to be permanent.

Conclusions relating to the Occurrence of Intestinal Putrefaction in Epilepsy.—Before we undertake to point out the conclusions of be drawn from a study of the facts relating to intestinal putrefaction in the cases of epilepsy that are here presented, it is desirable to indicate the nature of the evidence on which these conclusions are based.

Before the use of scientific methods in medicine digestion was regarded wholly as a putrefactive process. Early observers, however, pointed out the error of this view. As was shown by recent investigations of Harris and Tooth,* normal digestion in the stomach is always free from bacterial action. But in the intestine, while the ferments of the various secretions are giving rise to those changes that are essential for the absorption of food, putrefactive processes always occur and possibly aid in digestion. The bacteria which are the immediate cause of this putrefaction are introduced with the food and escape the destructive action of the gastric juice.

This intestinal putrefaction is kept within normal limits by certain natural antiseptic conditions. The action of the bile in this direction is well known. Its power of diminishing putrescence is due chiefly to the fact that by increasing peristalsis it hastens the passage of its contents through the intestine.† The acid of the gastric juice has an anti-

* *Journal of Physiology*, ix, p. 220; see also in this connection Straus and Wurtz (*Archives de méd. expérimentale*, 1890).

† Ueber den Einfluss von Magengährung auf die Fäulnissvorgänge im Darmkanal. *Archiv f. experim. Pathologie u. Pharmakol.*, Bd. 26, S. 133–138.

septic action on the contents of the small intestine, as has been recently shown by Wasbutzki.* The tendency of micro-organisms to produce compounds which, if allowed to accumulate, would ultimately destroy their own life, is of interest in this connection.

Thus we find in the intestine, under perfectly normal conditions, two distinct kinds of ferment action by two widely different orders of ferments, which give rise to the formation of products of entirely different nature. On the one hand the unorganized digestive ferments produce changes in the food preparatory to absorption. They form from albumin, aided by the alkaline medium in which they act, successively an albuminate (alkali-albumin), albumoses, and true peptones, which latter may yield in part leucine, tyrosine, asparaginic acid, ammonia, and proteinchromogen. On the other hand, the organized ferments—the bacteria—yield by their action on proteids, or on the products into which the proteids have already been transformed by the digestive action of the unorganized ferments, the following substances or classes of substances: ammonia, sulphureted

* Wasbutzki found that the excretion of ethereal sulphates was increased when the secretion of hydrochloric acid in the stomach was diminished in consequence of gastric disease. He found further that in cases of hyperacidity of the stomach the excretion of ethereal sulphates was diminished. This he attributes to the action of lactic and butyric acids.

See also in this connection Bierhacki (Ueber die Darmfäulniss bei Nierenentzündung und Icterus nebst Bemerkungen über die normale Darmfäulniss. *Deutsches Archiv für klinische Medicin*, Band 49, 1. Heft, 1891).

This author found that in cases of Bright's disease (chronic diffuse nephritis) in which the secretion of hydrochloric acid is diminished there is a corresponding increase of the ethereal sulphates in the urine.

In cases of catarrhal jaundice with complete occlusion of the bile-duct he found a similar increase in ethereal sulphates, and he regards this fact as evidence that the bile has an antiseptic action.

hydrogen, ammonium sulphide, volatile and fatty acids, amines and amido-acids, especially leucine and tyrosine; indol, skatol, phenol, cresol, phenyl-propionic and phenyl-acetic acids, and the aromatic oxyacids hydroparacumaric acid and parahydroxyphenylacetic acid.*

The presence of these numerous acid compounds, especially of lactic acid, gives the contents of the large intestine, as a rule, an acid reaction. Further, intestinal bacteria have a fat-splitting action similar to that of the steapsin of the pancreatic juice, giving rise, however, in addition, to lower acids of the fatty series. Likewise lecithin is decomposed into glycerophosphoric acid and the ptomaine choline, which further breaks up into carbonic acid, marsh gas, and ammonia.

Besides this long and varied list there are doubtless other substances which may result from bacterial activity in the alimentary canal, of which nothing is directly known, but which may nevertheless play an important part in the condition of the subject. It is held by some observers that the production of poisonous alkaloids in the intestine is a normal process and that these are absorbed, and, if excessive in amount, may lead to auto-intoxication. There is some evidence that this is the case in certain forms of disease.

That many of the products of intestinal putrefaction are absorbed is well known. They are, however, rapidly excreted by the kidneys, so that the individual generally escapes their poisonous action. In the urine these substances appear in but slightly modified forms, and their amount and nature may reveal the condition in the intestine. Several methods are available for estimating putrefactive changes from a study of the urine. Thus Brieger † estimated the

* See Haliburton, *Text-book of Chemical Physiology and Pathology*, 1891, p. 694.

† *Zeitschrift f. physiolog. Chemie*, Bd. 11, S. 221.

quantity of phenol from the distillate of acid urine. The quantity of indigo-blue * which the urine yields may also serve as an index to these changes.

These methods, however, are open to objection, since they take into account only one of the many possible products of putrefaction which may be present. These products exist in the urine in combination with sulphuric acid as ethereal potassium sulphates. Thus phenol, cresol, catechol, indol, skatol, etc., which are formed in the intestine appear in the urine as phenolsulphate of potassium, cresol-sulphate of potassium, catecholsulphate of potassium, indoxylsulphate of potassium, skatoxylsulphate of potassium, etc. An estimation of the amount of sulphuric acid in this ethereal combination gives, therefore, a more nearly correct indication of the amount of these substances present, and hence of the putrefaction in the intestine. Putrefactive processes outside the alimentary canal, putrid cystitis, putrid abscesses, putrid peritonitis, etc., have the same result as putrefactive processes within the intestine. The amount of the ethereal sulphates is in a general way proportional to the degree and extent of the putrefactive processes.

We may now indicate a little more fully the character

* This is often a very unreliable index to the degree of intestinal putrefaction, for there is no necessary relation between the amount of indican in the urine and the quantity of the ethereal sulphates. Only a small number of our cases of epilepsy in which the sulphates were in marked excess showed an excess of indican. In our experience, a large excess of indican (30 to 80 milligrammes) has been met with chiefly in cases which showed symptoms of chronic intestinal catarrh. Regarding the occurrence of indican see the following: Jaffé (*Arch. f. gesammte Physiologie*, Bd. 30, S. 483), Senator (*Ctrbl. f. d. medicinische Wissenschaften*, No. 20-22, 1877), De Vreis (*Ueber Indican in Harn*, Kiel, 1879), Henninga (*Deutsch. Arch. f. klin. Med.*, Bd. 23, S. 271-287), Filati (*Gazzetta chimica italiana*, vol. xiii, p. 378).

of the evidence on which this relation between ethereal sulphates in the urine and putrefaction within the intestine is based.

It was at one time held that the aromatic substances in combination with the sulphate were derived directly from aromatic constituents of the food. But while this may in exceptional instances and to a limited extent be true, especially in herbivora, in the case of animals like dogs and man, who live on a mixed diet containing little or nothing of an aromatic nature, this possible origin has failed to explain the regular presence of these aromatic substances in the urine. Next, the various tissues themselves came to be regarded as the seat of their formation, and there seemed to be considerable support for this view. In starving dogs Salkowski* found considerable quantities of indoxyl potassium sulphate (indican) present in the urine. Likewise, R. van der Velden† found the ethereal sulphates reduced only one half when the animal was kept entirely without food for five or six days. Both Ewald‡ and Baumann,# however, working upon cases of intestinal fistula in man, found that when the intestinal contents were withdrawn through the fistula the aromatic substances almost entirely disappeared from the urine. They further found that when the fistulous opening was closed and the intestinal contents were made to pass through the entire length of the intestine these substances reappeared in the urine in the usual amounts. Kühne and Nenki have shown that these aromatic bodies, especially indol, come from the putrefaction of proteids. Artificial pancreatic digestions of albumin were found to

* *Berichte der deutsch. chem. Gesellschaft*, Bd. ix, S. 408.

† Ueber die Ausscheidung der gepaarten Schwefelsäuren im Harn. Virchow's *Archiv*, Bd. 70, 1872.

‡ *Arch. f. pathol. Anat.*, Bd. 75.

Zeit. f. physiolog. Chemie, Bd. x, 1886.

yield considerable quantities of indol, but when bacterial action was prevented by thymolization, indol and other aromatic putrefactive products were entirely absent.

Thus there is satisfactory evidence that these products, which are formed from the decomposition of proteids in the intestinal canal by the activity of micro-organisms, are absorbed, and are ultimately excreted by the urine. In confirmation of this is the influence on the separation of ethereal sulphates which is exerted by antiseptics when introduced into the intestine. As shown by Baumann* and Morax,† putrefaction can be checked in the intestine of the dog by inanition together with the administration of large doses of calomel or iodoform. Under these circumstances a concomitant disappearance of ethereal sulphates in the urine was noted. In man it is not possible to administer sufficiently large doses of these drugs to produce this result. Rovighi,‡ working in the laboratory of Baumann, has recently shown that the administration of terpenes and camphors,§ in the case both of men and dogs, diminished the separation of ethereal sulphates to only a moderate extent in men, but considerably in dogs. It is interesting to note in this connection that, as pointed out by Rovighi, there are variations in the separation of the ethereal sulphates at different

* Baumann and Wassilieff. *Zeitsch. f. physiolog. Chemie*, Bd. 6, S. 112.

† Bestimmungen der Darmfäulniss durch Aetherschwefelsäuren im Harn. *Zeitsch. f. physiolog. Chemie*, Bd. x, S. 318, 1886.

‡ Die Aetherschwefelsäuren im Harn und die Darmdisinfection. *Zeitsch. f. physiolog. Chemie*, Bd. xvi.

* Rovighi (*loc. cit.*) experimented also with kumyss. He found that by taking 1·5 litres of kumyss daily for five days the ratio of his sulphates was reduced from 10·7 to 20. He does not state whether he took other food at this time, but it is presumed that he did. The decided influence of the kumyss is probably to be referred to the lactic acid it contains.

hours of the day. Their separation is greatest during the day, more especially after meals. This fact illustrates the importance of drawing conclusions only from the examination of the twenty-four hours' urine.

The amount of putrefactive products in the urine is directly related to the amount of proteid food ingested, and it is important to consider this factor in drawing conclusions as to the degree of putrefaction that is going on. The total sulphates of the urine run parallel to the elimination of nitrogen.* Hence they indicate in a general way the extent of nitrogenous metabolism, which is directly dependent on the amount of nitrogenous food absorbed. Thus, by a comparison of the sulphates in ethereal combination with the other (so-called preformed sulphates) sulphates of the urine, we have an index of the degree of intestinal putrefaction, without further consideration of the amount of proteid food ingested. It is usually stated that under normal conditions the relation between the ethereal and preformed sulphates is about one to ten.† But, while this may represent in general terms the normal relation, it is liable to fluctuation with the nature of the food. On a diet composed of vegetable proteids the proportion of ethereal sulphates may be somewhat increased (one to eight), while on a milk diet the ratio normally falls very much (one to twenty or less).

We may now pass to the consideration of the results obtained from the study of the products of intestinal putrefaction in our cases of epilepsy. We may begin with

* We have found in a large number of cases, both epileptics and non-epileptics, that the ratio of the total sulphates to the urea is singularly constant, being usually from 1 : 10 to 1 : 13.

† Hoppe-Seyler. Ueber die Ausscheidung der Aetherschweifelsäuren im Urin bei Krankheiten. *Zeitschr. f. physiol. Chemie.* Also R. van der Velden, *loc. cit.*, Bd. xii, S. 1, 1888.

the examination of the *grand mal* cases, for these are greatly in the majority, and show the most pronounced deviations from the normal.

Taking first the sulphates (since, as we have seen, they are the safest general indication of the degree of intestinal putrefaction), we observe that a very large proportion of our cases show a higher ratio of the ethereal to the preformed sulphates than is observed in health. It is convenient to group the cases of *grand mal* according to the degree to which the sulphates deviate from the normal. Of the twenty-nine cases, only two (V and XX) can be called distinctly negative; six (Cases IV, VI, VII, XIII, XVII, and XXIV) are classified as doubtful, because the results are not sufficiently distinctive, either of health or disease, to enable us safely to interpret them; three (Cases VIII, XVI, and XXV) are classified as giving decided results, and all the rest, nineteen in number, as giving results that are very marked.

It is important to note that on some of the days on which the ratio of the sulphates is excessively high the total amount of ethereal sulphates is distinctly high, while in other cases it is low. Thus, in Case I, on January 21st, the ratio of sulphates is 2·7, and in Case II, on January 5th, it is 3·2. Both these ratios are very high and nearly equal, but in Case I the total ethereal sulphates are 53·3 milligrammes, while in Case II they are 16·2 milligrammes. That is, in Case I the ethereal sulphates are present in more than three times the quantity than in Case II. Is the significance of these ratios (2·7 and 3·2) approximately the same notwithstanding the great difference in the total quantities of the ethereal sulphates? In interpreting our results are we to give most weight to the ratios of the sulphates or to the total ethereal sulphates? While we ought to be guided mainly by the ratios, we must in some cases

take into consideration also the totals.* In the instances that have been cited the ratios are so high that we can not doubt that they were caused by excessive intestinal putrefaction in both cases, for, though in Case II the total ethereal sulphates were only 16.2 milligrammes—an amount usually quite within the limits of health—we must regard this as excessively high in the presence of so small an amount of the preformed sulphates as is here present (52.5 milligrammes). This amount (52.5 milligrammes) of preformed sulphates is less than is usually observed in health, and depends on the fact that only a small amount of nitrogenous food has been assimilated. We know, however, that when the preformed sulphates are reduced to this amount in *health*, the combined sulphates are correspondingly reduced, a relation of about 1 to 10 being maintained. When, therefore, we find that the ethereal sulphates are *not* correspondingly reduced, as in Case II, we have no hesitation in pronouncing the figures distinctly abnormal.

There are many instances, however, in which it is almost impossible to decide whether or not a case deviates from the normal. Thus, in Case XIII we find two ratios—11.2 and 8.7—the former certainly normal, the latter a little high, but not positively outside the limits of health. In this case the ethereal sulphates are small in amount (17.9 milligrammes for two days), and this leads one to question whether the ratio of 8.7 is to be regarded as distinctly abnormal. The case has therefore been classed with the doubtful ones.

* The totals vary so enormously in healthy adults (100 milligrammes to 300 milligrammes in the day) that the importance of relying on the ratios is especially impressed upon us. The establishment of a standard in health for the ethereal sulphates involves considerations very similar to those that apply to the establishment of a criterion of uric acid excretion. See *N. Y. Med. Jour.*, June 4, 1892.

Having established the fact that a majority of our cases give unmistakable evidence of an excessive formation of putrefactive products in the intestine, it remains to consider whether the excess of these products is or is not to be regarded as bearing a relation to the occurrence of the epileptic seizures. If in any given case in which there are evidences of excessive intestinal putrefaction a more or less constant relation exists between the degree of this excess and the frequency or character of the seizures, such a relation may reasonably be considered evidence of something more than coincidence, and the more constant the relation the more strongly does it suggest a dependence of the seizures on toxic substances produced by the excessive putrefaction in question. Before attempting any generalizations, we may advantageously take up certain cases with a view to seeing what they teach regarding such a relation.

One of the first seizures that is available for the present inquiry is that which occurred in Case I, on January 25th. On January 21st the ratio of the sulphates was higher than at any period recorded in this case—namely, 2·7; on the day of the seizure it was 4·4, and on the day after it was 7·6. The ratio on the 22d, immediately before the seizure, is unfortunately unknown. Between December 9, 1891, and January 21, 1892, there are nine estimations of the sulphates, which for this period give a ratio much nearer the normal than for the period just before and at the time of the seizure. In the six weeks mentioned there was one paroxysm only (January 2d). It is to be noted that on January 21st the amount of indican (which is regularly present greatly in excess) was 56·9 milligrammes—that is, higher than at any time between December 5, 1891, and January 23, 1892, with one exception (January 1, 1892), when the indican reached 57·3 milligrammes, but when the sulphates give a less abnormal ratio (7·9) than those above

noted. On December 1st the patient began to take sodium salicylate. Between December 1st and December 8th he took fifteen grains three times daily. From December 8th until January 27th he took ten grains three times daily, the bromides being continued. On December 6th the ratio of the sulphates was 13—*i. e.*, within the normal. On December 9th it was 7·3, but the quantity of indican was very low indeed (possibly within the normal), and much lower than during October and November, when the patient was having frequent seizures (about once a week). The quantity of indican remained relatively low (as compared with October and November) until January 1st, when it rose to 57·3 milligrammes. The day following there was a mild seizure, but during the entire month of December there was not one. On the day before this seizure the sulphates gave a ratio of 7·9, a much higher ratio than the average of the days preceding. On the day of this seizure the ratio of sulphates was 6·4 and the indican 45·3 milligrammes. It is true that on January 4th there was a ratio of 3·9 and no seizure, but the indican was distinctly lower than on the days of the two seizures we have mentioned.

The patient had another seizure on February 3d. On this day the ratio was 9·1, but the ethereal sulphates were in large amount (373 milligrammes), and the indican was very high (69·5 milligrammes).

On March 31st the patient went on an almost exclusively milk diet, which had the effect of greatly reducing the ratio of sulphates and of somewhat diminishing the frequency and severity of the seizures. The seizures during this period were but imperfectly studied, and we can not safely draw conclusions from them, but it is interesting to note that the ratio for the day of the seizure of the 28th of April was 11·6. This ratio would ordinarily be regarded as belonging to health, but it is much higher than should be ob-

served in an individual upon a milk diet (1 to 20). On May 6th the ratio was 10·6, and for the first time in our knowledge of the case indican was almost wanting. On May 9th there was a strong indican reaction, and on May 10th there was a strong indican reaction and a seizure.

In this case, therefore, there was a general correspondence between the seizures and the degree of putrefactive action in the intestine. When the salicylates were first given they exerted a check upon the products of intestinal putrefaction, and during this time seizures were absent. As soon as this antiseptic effect wore away (as shown by the reappearance of the products of putrefaction in excess) the seizures recommenced.

In Case II there was a seizure on January 5th, when the ratio of sulphates was high (3·2). On January 14th there was another seizure, and on January 12th the sulphates were again high (4·9), and a considerable amount of indican was present. On the day following the seizure the ratio of sulphates was considerably lower (7·8), and the total ethereal sulphates were less in amount than on either the 1st or 12th. Two seizures occurred on June 30th, but, as observations were made only on the 25th and the 28th (when the ratios were high—3·5 and 5·1), we can not reach any conclusion in the case of these paroxysms. A seizure occurred on February 15th, when the sulphates were not very high relatively or absolutely. In general, however, we may say that the ratio of sulphates has run unusually high in this case about the time of seizures—*i. e.*, just before or at the time of the seizures. But it is to be regretted that so few observations were made in the interparoxysmal periods.

In Case XIX we have a ratio slightly higher on the day of the seizure than on the day before or after. The total amount of ethereal sulphates was considerably higher on the day of the paroxysm than on that before or after.

In Case XXI the ratio was 5·6 on the day of the seizure, 5·9 on the day before, and 5·7 on the day after. The ethereal sulphates were slightly greater in amount on the day of the seizure and on the day before than on the day after.

In Case XXII the ratio was 5·9 on the day of the seizure, 9·9 on the day before, and 6·5 on the day after. On the day of the paroxysm the total ethereal sulphates were greater than on the day before, but about the same as the day after. The seizure in this case was a slight one, consisting of loss of consciousness and slight general tonic spasm, but without clonic spasm.

In Case XXIII the ratio was 6·6 on the day of the seizure and on the day before. On the day after it was 6·8. The ethereal sulphates were greatest in amount the day before the seizure, and were greater on the day of the seizure than on that following it. But the differences in the ratios are so slight that the case is not conclusive as regards the particular point of our present inquiry.

In Case XXIV the ratio was 4·4 on the day of the seizure, 6·6 the day before, and 11·4 the day after. The ethereal sulphates were about twice as abundant on the day of the seizure as on the day before or the day after.

In Case XXVIII the ratio was 5·0 on the day of the seizure, 4·2 on the day before, and 5·9 on the day after. The ethereal sulphates were greater in amount the day before and the day after than on the day of the seizure. It is difficult to interpret the figures in this case.

The cases of *grand mal* which have not been mentioned in the foregoing enumeration were not available for the inquiry in point, either because the seizures were too numerous, because drugs were given which are thought to affect intestinal putrefaction, or because no individual seizure was carefully studied in its relations to the interparoxysmal period.

In Cases X and XIV sodium salicylate was given in doses of ten grains three times daily (the bromides being continued) for seven days, to see whether they diminished the products of intestinal putrefaction and concomitantly the number of epileptic seizures. In Case X the results were negative in that the drug failed to exert an appreciable effect upon either the products of putrefaction or the seizures. In Case XIV, however, there was a pronounced diminution in the ratios of the sulphates at the time the drug was given and a distinct diminution in the number of seizures. But the ratio of sulphates was not brought inside the limits of the normal, and the seizures, though reduced in frequency, continued numerous.

This observation, together with that made upon Case I, shows that a reduction of the products of putrefaction by means of sodium salicylate is likely to be associated with at least a temporary reduction of the number of seizures.

It was determined to see whether it is possible to increase the products of putrefaction experimentally and concomitantly the number of seizures. For this purpose it was decided to make use of considerable doses (twenty grains) of sodium bicarbonate, it having been shown by Stadelmann * that in health the antiseptic action of the gastric juice may be diminished by alkalies, with a consequent increase of the products of intestinal putrefaction. The results of our experiments were as follows:

In Case XVI, ten grains of sodium bicarbonate, three times daily, were given for five days, and then twenty grains, three times daily, were given during five days more. During these ten days the patient had ten seizures, eight of them occurring during the first five days of the period.

* Ueber den Einfluss der Alkalien auf den menschlichen Stoffwechsel. *Bericht über die Verh. des IX. Congresses.* Abstract in *Centralblatt f. klin. Medicin*, 1890, No. 27.

During the thirty days preceding this seizure the patient had eleven seizures only—*i. e.*, she had about the average number for an entire month. Reference to the table shows that during the period when the soda was given the ratio of sulphates was very greatly increased as compared with the preceding days. The total ethereal sulphates were also markedly increased, but it is interesting to note that this increase is confined to the first period of five days when the seizures were most numerous. It should be noted also that the urea excreted was very small in amount while the soda was being taken, this being due, no doubt, to the loss of appetite caused by the administration of the salt. It is possible that this greatly diminished assimilation of nitrogenous food, as shown by the diminution in urea, had a tendency to diminish the number of seizures rather than to increase them. It would be interesting to know what would have been the effect of the sodium salt upon the seizures and upon the ethereal sulphates had the assimilation of nitrogen been maintained at the level of the days preceding the experiments.

In Case XXV sodium bicarbonate was given in doses of fifteen grains, three times daily (with meals), for seven days. During this period there were two seizures—one on each of the last two days. Two consecutive seizures have not been noted before in this patient. During the period when these seizures occurred the ratios ran higher than usual, and the total ethereal sulphates were somewhat increased. In the week following the discontinuance of the sodium bicarbonate (perhaps longer) there was no seizure, and the ratios ran very nearly normal.

In Case XIV twenty grains of sodium bicarbonate were given for five successive days, soon after the administration of sodium salicylate for six days. Putrefaction was unquestionably increased, as is shown both by the total

ethereal sulphates and by the ratios. The number of seizures, however, continued small. This is in direct opposition to what we should have expected. No definite conclusion can be drawn as to the effect upon seizures of the increased putrefaction induced by the administration of sodium bicarbonate, since the evidence from the three experiments is conflicting.

The study, therefore, of our twenty-nine cases of *grand mal* shows that in twenty-one cases there was present unmistakable evidence of excessive intestinal putrefaction. Furthermore, a large proportion of the cases in which the observations were of such a character as to render a comparison possible, showed at least a general correspondence between the seizures and the degree of intestinal putrefaction as gauged by the analysis of the urine. This correspondence has been sufficiently close, in our judgment, to warrant the suspicion that intestinal putrefaction may play an important part in determining the occurrence of epileptic seizures in some cases of epilepsy—perhaps in a considerable proportion of cases. More than this we are unable to say at present, for those of our observations that relate to the concomitant variations of seizures and products of putrefaction are too few in number to permit a statement regarding epileptic seizures in general, although they appear convincing as regards most of the cases that have been studied.

We may conclude, then, that the excess in the products of intestinal putrefaction which we have noted is a characteristic of a considerable proportion of all cases of idiopathic *grand mal*, for the number of our cases is sufficiently great to exclude the possibility that our results depend on the mere coincidence of intestinal derangement and epilepsy which one might expect occasionally to meet. Nevertheless the question arises, How does it happen that so

many cases of epilepsy give evidence of this abnormal condition? Is it not possible that there may be some peculiarity about the life of the epileptic which predisposes him to excessive intestinal putrefaction? Two possible sources of error in the interpretation of results suggest themselves in this connection: First, peculiarities in diet; and, second, the influence of bromides.

As regards the possible dependence of our results upon any peculiarity in the diet of our patients, it may be said that no peculiarity existed such as would account for these results. It is possible that the use of a large proportion of nitrogenous food, such as readily undergoes putrefaction (especially vegetable nitrogenous food), might bring the ratios of the sulphates within the pathological limits, but none of our cases were known to be upon such a diet. These cases were, moreover, drawn from several different sources, and it is hardly to be thought of that the same unusual dietetic condition should have been operative in each of these groups of cases. Again, in several of our cases the dietary was one which included a minimum of nitrogenous food, and these cases are among those that show the greatest deviation from the normal in the products of putrefaction. We can not, therefore, seriously entertain the idea that the diet in our cases affords an explanation of the results.

The possibility that our results may depend, in part at least, upon the influence of bromides is not so easily to be disposed of. Almost all of the cases of epilepsy were taking bromides at the time of our study and for a considerable period before, and one might hold, with some plausibility, that this circumstance invalidates the interpretation of results, since there is reason to think that long-continued, large doses of the bromides may give rise to intestinal disorder, and very possibly to excessive intestinal putrefac-

tion.* As we have been able to find few epileptics in whom this possible influence of the bromides can be ruled out, it is difficult for us to give direct proof that no such influence was exerted in the cases that have been under consideration. The question really resolves itself into one of probabilities, and it is believed that the following considerations render it in the highest degree improbable that the bromides are responsible for the evidences of putrefaction that have been dwelt upon :

First. The quantity of the bromides taken in our cases was moderate (twenty to eighty grains per day—the “mixed” bromides being used in many cases), and there is no evidence that moderate doses of the drug give rise to intestinal putrefaction, either directly or indirectly, whatever may be the case with very large doses † (three to four drachms in twenty-four hours).

Second. As already stated, in the cases where comparison was possible the evidences of intestinal putrefaction were distinctly greater about the time of the seizures than in the intervals, notwithstanding the fact that the bromides were given in equal doses from day to day. This increase in the products mentioned at the time of seizures could hardly be explained by any known effects of the bromides.

Third. As already stated, seizures have been controlled by influences which coincidently controlled the products of putrefaction. It is impossible to explain this fact on any theory connected with the action of the bromides.

Fourth. There are among our cases of epilepsy several (IV, XXIX, and XXX) in which bromides have been taken in moderate doses for a long period of time, but in which there is no evidence of excessive putrefaction in the

* Féré. Bromuration et antisepsie intestinale. *Nouvelle iconographie de la Salpêtrière*, 1890, p. 349.

† See Féré (*loc. cit.*).

contents of the intestine. On the other hand, there are among the cases two (VI, XXVI) in which the patient has had no bromides for many months, but in which the putrefactive processes nevertheless run high.

In view of these facts, it must be admitted that we are unable at present to offer any explanation of the pathological conditions noted in our cases of epilepsy; we can not say why there should occur in epilepsy so considerable a proportion of cases in which there are evidences of excessive intestinal putrefaction. It is possible that future research will determine the nature and significance of the relation.

While we can not profess that we have proved that the epileptic seizure is ever the consequence of abnormal putrefactive processes in the intestine, we have at least obtained evidence which forcibly suggests that epileptic seizures are sometimes the consequence of toxic substances produced in the intestinal canal, and that the formation of these substances is related to processes of a putrefactive nature. It is of course evident that no pretense is made to having discovered the cause of epilepsy. If, as we suspect, intestinal putrefaction plays a *rôle* in the causation of some cases of epilepsy, it is certainly operative only in determining seizures, and probably acts in most cases, and perhaps in all, upon that predisposition to the excessive liberation of nerve force, either hereditary or acquired, which we must recognize as by far the most powerful factor in the causation of the disease.

A very interesting question presents itself in connection with the facts we have brought forward. Do cases of epilepsy which rest on an organic basis differ in any way from idiopathic cases as regards the evidence that toxic substances formed in the intestine may operate in determining seizures? Much more extended observation is necessary

before this question can be answered. Yet it is of interest to note that of the three cases of *grand mal* in which there was some reason to suspect organic disease, one was negative and two were doubtful as regards the evidences of excessive intestinal putrefaction. Regarding the possibility of a difference between *grand mal* and *petit mal* there is little to be said. It should be noted that in two cases of *petit mal* where the seizures were very frequent (in one of these cases there were occasional *grand mal* seizures) there were no evidences of intestinal putrefaction, and that in a third case, in which the seizures were exclusively of the *petit mal* type, the indications were doubtful or negative.

We have made no systematic study of the influence of intestinal antiseptics in diminishing the number or modifying the character of epileptic seizures. Judging from a limited experience with salicylate of sodium, there is some reason to think that we may exert a beneficial influence, at least temporarily, upon some cases of epilepsy, by the use of drugs that are thought to control bacterial activity in the intestine. But before anything further can be said about the possibility of thus modifying the course of epilepsy in even a limited proportion of cases, it is essential that there should be carried out an extended and carefully planned series of observations upon the action of the various drugs of the class mentioned.*

NOTE.—It is interesting to note the large number of cases in which dark (black) urines were obtained—*i. e.*, urines which when voided appeared normal, but on becoming alkaline and on exposure to the air

* Some work has been done upon the influence of drugs upon the excretion of the ethereal sulphates in human subjects. Thus Ortweiler (Physiolog. und patholog. Bedeutung des Harnindicans, *Mittheil. d. Würzburger medic. Klin.*, Bd. 11, S. 153, 1888) found that in six cases of intestinal disease naphthaline had very little influence in checking putrefaction. R. Steiff (Ueber die Beeinflussung der Darmfäulniss

acquired a dark color, first forming a black zone at the exposed surface of the liquid. This appearance is known to be due to the presence of hydroquinone and pyrocatechin, two aromatic substances formed by intestinal putrefaction. Although no attempt has been made to study the urine in regard to this particular point, the formation of the dark color was noted in Cases XIV, XV, XVI, XVIII, XXI, and XXVIII. Several other cases, studied earlier, gave the same appearance, but no importance was then attached to the peculiarity.

Sulphates were determined by the Salkowski-Baumann method; urea by Pflüger's modification of Liebig's method or from the total amount of nitrogen as estimated by the Kjeldahl method; uric acid by the Ludwig-Salkowski method; indigo-blue by Jaffé's gravimetric method; phenol after the method of Koppe-schaar; and oxy acids after the manner described by Baumann.

durch Arzneimittel, *Zeitsch. f. klin. Medicin*, Bd. 16, S. 311-324) found that doses of 0·3 gramme of calomel, three times daily, did not diminish the ethereal sulphates. Equal doses of camphor caused a slight reduction in the excretion of the ethereal sulphates. Rovighi (*loc. cit.*) found that oil of turpentine and camphor exert a moderate effect on intestinal putrefaction in man. Carlsbad salts at first increased the ethereal sulphates excreted, but subsequently diminished them. Kumyss he found to exert a very marked influence in the elimination of the ethereal sulphates.



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